

REMARKS

In response to the office action mailed on January 25, 2008, Applicants submit the following remarks. Claims 1, 3-15, 17-27, 29-33, and 35-37 are pending.

The Examiner rejected claims 1, 3-10, 15, 17-27, 29-31 and 35-37 under 35 U.S.C. §103(a) as being unpatentable over Smith et al., US 5,888,930 ("Smith") in view of Gray, PCT/AU2001/001370 ("Gray"), in view of Kaminski et al., US 6,015,542 ("Kaminski").

Claims 1, 3-10, 15, 17-27, 29-31 and 35-37 cover particles that include a cross-linked polymer matrix. The particles also include a first region including pores having a first predominant pore size and a second region surrounding the first region and including pores having a second predominant pore size, where the first predominant pore size is larger than the second predominant pore size. Smith does not disclose or render obvious such particles.

Instead, Smith discloses a micro-porous particle made of a polymer that is soluble in a suitable solvent and insoluble in water. Smith describes his particle and the material suitable for making his particles as follows:

The beads of the present invention are made of film-forming polymers, they have a generally spherical shape with diameters ranging from about 5 microns to about 5 mm, and they have a unique, continuously-gradated asymmetric microporous structure, with small pores near the surface and progressively larger pores toward the interior core. They are typically loaded with active ingredient following preparation of the beads, and the active ingredient is released at a slow and substantially constant rate over an extended period of time. (Smith, col. 2, lines 47-56.)

Useful polymers must be soluble in a suitable solvent and insoluble in a liquid that is miscible with the solvent. Typical polymer concentrations in the polymer solution are from 50 to 300 g/L. Solvents useful in the present invention must dissolve the polymer and be miscible with the liquid, typically water, used for precipitation. (Id., col.2, line 67-col.3, line 5; emphasis provided.)

To make the particles with the desired features, Smith further teaches a process that involves dissolving a polymer in a solvent other than water, spraying droplets of the resulting solution into a stirred precipitation bath that contains water, collecting the particles, and drying the particles.

In this regard, Smith reads:

The key to achieving the characteristic continuously-gradated asymmetric pore structure of the beads of the present invention is keeping the rate of solvent exchange with the liquid of the precipitation bath slow following a rapid initial precipitation that forms the "skin" layer. (Id., col. 3, lines 6-10.)

In order to achieve the continuously-gradated pore structure of the beads of the present invention, the polymer, its solvent, and the precipitation bath must all be specified. Examples of polymer/solvent bath combinations that result in asymmetric microporous beads of the invention include: polysulfone/dimethylformamide/water, polyvinylidene fluoride/dimethylformamide/water-dimethylformamide; polyvinylchloride/dimethylformamide/water dimethylformamide; polyurethane/dimethylformamide/water; and cellulose acetate/dichloromethane-dimethylformamide/water.

The beads of the present invention are prepared by first dissolving the polymer in a solvent or solvent mixture, then spraying droplets of the solution thus formed into a stirred precipitation bath containing a liquid, typically water, that is miscible with the solvent, allowing the precipitated beads to remain in the bath until substantially all of the solvent has been removed or exchanged, and then collecting the beads and drying them, if desired. (Id., col. 3, lines 49-67.)

Accordingly, after reading Smith, one skilled in the art would understand that, Smith's process does not involve forming a cross-linked polymer matrix. One skilled in the art would also understand that Smith discloses that his process, including, for example, the solvent, must be very carefully followed in order to obtain his particles. Thus, one skilled in the art would not have even wanted to try to modify Smith's process. Accordingly, it would not have been obvious to one of ordinary skill in the art to try to modify Smith's process to try to obtain the particles covered by the pending claims, and, even if such a person had tried to do so, the evidence of record (i.e., Smith's own disclosure) indicates that failure would have been the result.

In stark contrast to Smith, Gray describes a particle that is made of ion exchange resin and a radionuclide. The ion exchange resin preferably includes partially cross-linked aliphatic polymer. Gray also describes making such particles by incorporating the radionuclide into ion exchange resin particles. In this regard, Gray reads:

In particular, the present invention provides a particulate material as described above in which the polymeric matrix is an ion exchange resin, particularly a cation exchange resin. Preferably the ion exchange resin comprises a partially cross linked aliphatic polymer, including polystyrene. One particularly preferred cation exchange resin is the styrene/divinylbenzene copolymer resin commercially available under the trade name Aminex 50W-X4 (Biorad, Hercules, CA). However, there are many other commercially available cation exchange resins which are suitable. (Gray, pg. 6, lines 11-17.)

The ion exchange resin is preferably provided in the form of an aqueous slurry of microspheres of ion exchange resin having a particle size 30 to 35 microns, and the yttrium-90 sulphate solution is added to the slurry to absorb the yttrium-90 into the ion exchange resin microspheres. (Id., pg. 7, lines 13-17.)

Symmetrical microspheres of ion exchange resin (Aminex 50W-X4 cation exchange resin; supplied by 'Bio-Rad Cat # 1474313') with a diameter of approximately 30 to 35 microns are added to water (Water for Injections BP) to form a slurry that is then transferred into a reaction

vessel. Yttrium (90Y) sulphate solution is added to the reaction vessel and the mixture stirred at a speed sufficient to ensure homogeneity to absorb the yttrium (90Y) solution into the resin-based microspheres. (Id., pg. 9, lines 7-12.)

Therefore, Gray's ion exchange resin particles that include cross-linked polymers are provided commercially. Nowhere does Gray teach how to make his ion exchanges resin particles. Nor do Gray's particles have a first region including pores having a first predominant pore size and a second region surrounding the first region and including pores having a second predominant pore size, where the first predominant pore size is larger than the second predominant pore size.

As a result, one skilled in the art would not have wanted to combine Smith's process with Gray's process to somehow obtain the particles covered by the pending claims. Even if such a modification had been tried, there is no indication that the result would be the claimed particles.

In maintaining the rejection, the Examiner stated:

[T]he claims as amended recite a cross-linked polymer comprised in the particle. It is noted that Gray teaches that in a preferred embodiment the polymeric matrix is partially cross linked. (Office Action, page 8.)

However, as explained above, Gray's particles do not have the features that claims 1, 3-10, 15, 17-27, 29-31 and 35-37 include. Applicants also point out that the Examiner fails to address Applicants' argument that, at least because of Smith's teachings, one skilled in the art would not have even wanted to try to modify Smith's process based on Gray's teachings, and even if one skilled in the art had tried to do so, there is no indication that the result would have been the particles covered by claims 1, 3-10, 15, 17-27, 29-31 and 35-37.

Kaminski does not disclose or render obvious particles that include a cross-linked polymer matrix, where the particles also include a first region including pores having a first predominant pore size and a second region surrounding the first region and including pores having a second predominant pore size, and the first predominant pore size is larger than the second predominant pore size.

None of Smith, Gray or Kaminski, alone or in combination, discloses or renders obvious the particles covered by claims 1, 3-10, 15, 17-27, 29-31 and 35-37. Indeed, one skilled in the art simply would not have even tried to modify Smith's process based on the teachings of Gray

or Kaminski to result in the particles covered by the pending claims. Further, none of the references cited by the Examiner, taken alone or in combination, enables a method that would result in Applicants' claimed particles. Applicants therefore request reconsideration and withdrawal of this rejection.

The Examiner rejected claims 11-12 under 35 U.S.C. §103(a) as being unpatentable over Smith in view of Gray in further view of Ajay K. et al., *Extended preoperative polyvinyl alcohol microembolization of intracranial meningiomas: assessment of two embolization techniques*, AJNR 14, 571-582 (1993) ("Ajay"). Claims 11-12 cover particles that include a cross-linked polymer matrix, where particles also include a first region including pores having a first predominant pore size and a second region surrounding the first region and including pores having a second predominant pore size, and the first predominant pore size is larger than the second predominant pore size.

As discussed above, neither Smith nor Gray, alone or in combination, discloses or renders obvious such particles. Ajay does not cure the deficiencies of Smith and/or Gray. None of Smith, Gray, or Ajay, discloses or renders obvious the particles covered by claims 11-12, and there is no suggestion to combine these references to provide the particles covered by these claims. Applicants therefore request that this rejection be reconsidered and withdrawn.

The Examiner rejected claims 13-14 and 32 under 35 U.S.C. §103(a) as being unpatentable over Smith in view of Gray in further view of Atcher et al., US 4,970,062 ("Atcher"). Claims 13-14 and 32 cover particles that include a cross-linked polymer matrix, where particles also include a first region including pores having a first predominant pore size and a second region surrounding the first region and including pores having a second predominant pore size, and the first predominant pore size is larger than the second predominant pore size.

As discussed above, neither Smith nor Gray, alone or in combination, discloses or renders obvious such particles. Atcher does not cure the deficiencies of Smith and/or Gray. None of Smith, Gray, or Atcher, discloses or renders obvious the particles covered by claims 13-14 and

32, and there is no suggestion to combine these references to provide the particles covered by these claims. Applicants therefore request that this rejection be reconsidered and withdrawn.

The Examiner rejected claims 1, 3-15, 17-27, 29-33, and 35-37 on the ground of nonstatutory obviousness-type double patenting, citing eight commonly owned patent applications. In view of the other rejections to claims 1, 3-15, 17-27, 29-33, and 35-37, Applicants request that these rejections be held in abeyance.

Applicants believe that the claims are in condition for allowance, which action is requested.

Please apply any other charges or credits to deposit account 06-1050, referencing Attorney Docket No. 01194-458001.

Respectfully submitted,

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